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March 17, 1997

**VIA UPS OVERNIGHT**

Dr. Elizabeth Yetley  
Office of Special Nutritionals (HFS-450)  
Center for Food Safety and Applied Nutrition  
Food and Drug Administration  
200 C Street, S.W.  
Washington, D.C. 20204

0061 '97 SEP 19 P1:35

***Re: Fulfillment of Reporting Obligation  
under 21 U.S.C. § 343(r)***

Dear Dr. Yetley:

Pure Encapsulations, Inc.<sup>1</sup> ("Pure"), by counsel, hereby submits an original and two copies of its notice of statements of nutritional support in accordance with 21 U.S.C. § 343(r). Pure does so within thirty days of its first marketing products with which the statements are associated. Under section 343(r), companies are not only required to make such a reporting but also to retain substantiation for each such statement. In proof of its compliance with those requirements, Pure herein submits a representative sampling, but not all, of the scientific documentation it retains supporting of each statement. In accordance with the requirements of section 343(r), Pure includes the following disclaimer in boldface type, prominently displayed upon each piece of literature that bears the statements listed below: **This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.**

<sup>1</sup> The address for Pure Encapsulations, Inc. is 490 Boston Post Road, Sudbury, MA 01776

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1. **Product Name: Creatine monohydrate**

**Statement of Nutritional Support:**

Creatine monohydrate provides safe nutritional support for athletes seeking peak performance in short-duration, high intensity workouts. By supporting the body's natural ability to regenerate the primary energy immediately available to working muscle, creatine monohydrate has the potential to increase optimal work output in activities such as weight-lifting and sprinting.

Creatine phosphate acts as the primary resupplier of ATP levels for high intensity efforts lasting up to and around 25 seconds. Up to 95% of the body's total creatine content is stored in skeletal muscle, 60% of which is stored in the form of creatine phosphate. During muscle contractions ATP is hydrolyzed to adenosine diphosphate (ADP). Creatine phosphate regenerates ATP levels by breaking down and lending phosphate to the ADP. As the muscle recovers, it is converted back into creatine phosphate. Due to the important role creatine plays in recharging ATP levels, researchers and athletes are focusing on how they can raise levels of creatine in the body.

Neither creatine phosphate nor ATP can be directly supplemented in the diet. Creatine phosphate levels will increase, however, with a rise in total creatine levels. Creatine is manufactured in the body by arginine, glycine and methionine. In the diet it is found in meat, especially red meat, and also in small amounts from plants. A mixed diet supplies an average of 1 g per day, while a vegetarian diet relies almost exclusively on the body's ability to manufacture creatine. Higher levels of creatine can be derived from creatine monohydrate, a supplemental form of creatine which has been shown to raise total plasma levels of creatine.

A clinical study of 17 subjects demonstrated that creatine monohydrate supplementation increased the total creatine pool in muscle. The subjects were administered 5 g of creatine monohydrate four or six times a day for 2 or more days. Supplementation resulted in a significant increase in the total creatine content of the quadriceps femoris muscle. The average increase in total creatine levels was from 126.8 to 148.6 mmol/kg and creatine phosphate increased from 84.2 to 90.6 mmol/kg. The increase was the most substantial in subjects with a low initial total creatine content, increasing their levels to the upper level of the normal range.

It has been theorized that a limited supply of ATP is one of the major limiting factors in maintaining peak muscle performance. Clinical studies have demonstrated that increasing total creatine pools through supplementation can increase maximum performance for short-duration, high-impact efforts.

Twelve subjects performed 5 bouts of 30 voluntary knee extensions with 1 minute recovery periods between each bout. Subjects were tested for peak muscle torque production before and after treatment with either placebo or creatine. The treatment period lasted 5 days and consisted of a placebo 4 times a day or 5 g of creatine 4 times a day plus 1 g of glucose a day. Subjects who were administered the placebo demonstrated no difference in performance. In the creatine group, however, peak muscle torque production increased in all subjects during the final 10 contractions of exercise in bout 1, throughout the entirety of exercise bouts 2, 3, and 4, and during contractions 11-20 of bout 5 after supplementation. Researchers concluded that creatine supplementation increased the level of peak torque production during repeated bouts of maximal voluntary muscle contractions.

In a similar study, researchers divided sixteen subjects into two groups receiving either 20 g per day of creatine monohydrate or placebo (glucose) for a six day treatment period. Before and after the treatment period, subjects performed high-intensity exercise consisting of 10 six-second bouts on a cycle ergometer with a 30 second recovery period in between attempting to maintain a pedaling frequency of 140 revolutions per minute. There was no difference in exercise output between the two groups before the treatment period. After treatment, however, the group supplementing with creatine monohydrate displayed an easier time maintaining the target speed towards the end of each exercise bout than the placebo group.

A further study utilizing the same treatment protocol of 20 g creatine monohydrate or placebo for six days confirmed the above results. In this study, subjects performed 5 standardized 6 second bouts of high intensity exercise, and after a 40 second rest were tested for their ability to sustain high power output during a 10 second exercise period. Subjects who had been administered creatine monohydrate demonstrated a significant improvement in exercise output.

In order to maintain peak performance in short-term, high-intensity exercises such as weight-lifting and sprinting, the body must maintain its stores of ATP, energy immediately available to working muscle. Creatine monohydrate has been shown to increase total levels of creatine in muscle stores, including creatine phosphate, which recharges the continually rapidly diminishing levels of ATP. This safe nutritional supplement has been shown to increase work outputs during repeated bouts of high-impact exercise. It has the potential to increase the intensity at which athletes regularly train and, therefore, to increase the individuals' muscle strength and stamina.

See Exhibit A.

2. Product Name: Reduced Glutathione

**Statement of Nutritional Support:**

Glutathione is a key component of the antioxidant system which protects the body from radicals at the cellular level. Within the cells, it is present in two forms: reduced and oxidized glutathione (a healthy cell has significantly higher levels of the reduced form). Reduced glutathione is involved in the synthesis and repair of DNA, enhances the antioxidant activity of vitamin C, the transport of amino acids, and the detoxification of harmful compounds. In addition, an intracellular abundance of reduced glutathione, as compared to oxidized glutathione, helps ensure normal cell proliferation. *Reduced glutathione levels are essential for regulation of normal cellular growth and proliferation.*

See Exhibit B.

**3. Product Name: Alpha Lipoic Acid**

**Statement of Nutritional Support:**

Alpha lipoic acid is an exceptionally versatile nutrient; being both water and fat soluble, it is able to function in almost any part of the body. Alpha lipoic acid is manufactured in the body, but often times not in the amounts necessary to perform its many functions. Alpha lipoic acid is a potent antioxidant which neutralizes harmful free radicals and enhances the activity of vitamins C and E. A key component of the metabolic process, alpha lipoic acid produces energy in muscles and directs calories into energy production. In addition, this potent nutrient helps sustain normal blood sugar levels, supports the nervous system, and provides nutritional support for normal liver functioning. *Alpha lipoic acid is a multifunctional, versatile nutrient which plays a key role in the antioxidant network and the metabolic process.*

See Exhibit C.

**4. Product Name: Ascorbyl Palmitate**

**Statement of Nutritional Support:**

Ascorbyl palmitate is a highly bioavailable, fat soluble derivative of ascorbic acid. It possesses all the benefits of vitamin C, but, unlike the water soluble form, is able to be stored in the lipid cell membrane until the body is ready to put it to use. Vitamin C offers a wide range of support for the human body. It is a potent antioxidant and free radical scavenger. It supports the body's defense system by enhancing white blood cell function and activity, and increasing interferon levels, antibody responses, and secretion of thymic hormones. It is essential for the formation and maintenance of intercellular ground

substance and collagen. Vitamin C aids in the absorption of iron and the formation of red blood cells and converts folic acid to active folinic acid. It has histamine lowering properties, increases lymphocyte formation, and is required for the synthesis of carnitine and steroids. *Vitamin C, one of the most potent dietary antioxidants, provides optimal nutritional support to all physiological functions, including, notably, vascular and capillary integrity in support of the circulatory system. The ascorbyl palmitate form of vitamin C is stored in the lipid cell membrane, providing a ready store of this essential nutrient.*

See Exhibit D.

5. **Product Name:** ArthRed (hydrolyzed bovine collagen peptides for joint support)

**Statement of Nutritional Support:**

Hydrolyzed bovine collagen peptides (HBCP) have been the subject of several clinical trials in Europe for the support of healthy joint function. Specifically, HBCP has been shown to nutritionally support the inhibition of catabolic disintegration of the cartilage mass. HBCP improves nutrient and energy consumption by cartilage tissue, stimulating restructuring processes and encouraging the maintenance of a healthy collagen matrix. *ArthRed contains naturally occurring compounds the body needs to build and strengthen cartilage and promote healthy joint function. The results of clinical trials suggests the administration of 7-10 grams per day of HBCP for a minimum of six months. The beneficial nutritive effects of this supplement can be best achieved by making it a regular, permanent addition to the normal diet.*

See Exhibit E.

6. **Product Name:** Soy Isoflavones

**Statement of Nutritional Support:**

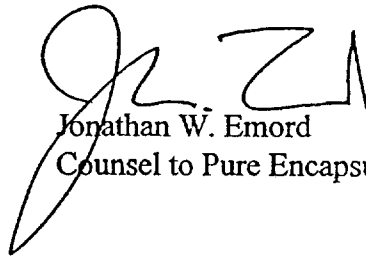
Soybeans and soy products such as tofu and tempeh are widely recognized for their health promoting properties. The principle active components are isoflavones, phytochemicals which have demonstrated antioxidant, antiangiogenetic, and estrogen activity. The isoflavones genistein and daidzein are potent antioxidants which promote and sustain the health of the body's immune system. In particular, soy isoflavones help insure the integrity of DNA against exogenous and endogenous stresses. As phytoestrogens, isoflavones exhibit weaker estrogenic activity than human estrogens but compete for the same receptor sites on human cells, thereby lowering the levels of circulating human estrogen. These phytoestrogens also increase growth hormone and

prolactin, decrease luteinizing hormone, and have beneficial effects on hormone-related bone decalcification. In addition to their estrogenic activity, soy isoflavones promote healthy cholesterol levels without lowering levels of the beneficial HDL cholesterol. *Soy Isoflavones provide a convenient way to supplement the diet with many health benefits of soy.*

See Exhibit F.

See attached Certification of Pure Encapsulations, Inc.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'J. W. Emord', with a large, stylized loop on the left side.

Jonathan W. Emord  
Counsel to Pure Encapsulations, Inc.

Certification

I, Ray Hamel, General Manager of Pure Encapsulations, Inc., hereby certify that the information contained in the foregoing notice is complete and accurate and that Pure Encapsulations, Inc. has substantiation that the above-listed statements of nutritional support are truthful and non-misleading.

Executed on: 3/17/97

Raymond F. Hamel  
Ray Hamel